PHARMACOLOGICAL EVALUATION OF NOOTROPIC AND NEUROPROTECTIVE ACTIVITY OF SESBANIA GRANDIFLORA EXTRACTS IN STREPTOZOTOCIN-INDUCED DIABETIC MODEL OF RATS

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Background: Diabetes Mellitus (DM) is a multifactorial disorder and is frequently correlated with chronic problems associated with various major organs. In recent times, there has been some correlations reported about the neurological complications of DM, such as cognitive impairment, vascular dementia, stroke, or depression, and observed that the brain tissue of the diabetic patients with hyperglycemia have shown injury at various locations with a varied profile of micro and macrostructural changes, which leads to the neurodegeneration, neuro-vascular deterioration, neuro-inflammation, and progressive cognition decline. Aim: The current study assesses memory enhancing activity of Sesbania Grandiflora (SG) extracts in streptozotocin (STZ)-induced diabetic model in rat.

Methods: The extracts (petroleum ether, ethyl acetate and methanol) were analyzed for acute toxicity and later its neuroprotective and memory enhancing activity in the selected rat model. STZ (55 mg/kg) injection was administered intraperitoneally to the animals to induce memory impairment. SG extracts were administered for 70 days after confirming STZ-induced dementia to detect its beneficial effect. To know the memory function the animals were subjected to Y-maze and Morris water maze test. After the tests, the animals were sacrificed and performed cholinergic function and oxidative stress with the brain tissue.

Results: It was observed that STZ caused significant memory impairment, which was significantly reversed by methanolic extract with 100 and 200 mg/kg. It was found that the cholinergic dysfunction, rise in lipid peroxidation levels were significantly (p<0.001) reduced. In the diabetic induced group, it was identified that there was a radical reduction of glutathione, superoxide dismutase, and catalase activities than the control group animals.

Conclusion: The current investigation established that SG leaf extracts improve the memory by enhancing the cholinergic transmission and reducing the oxidative stress in the brain of diabetic rats.

Keywords: Diabetes, dementia, cholinergic dysfunction, oxidative stress and Sesbania grandiflora.

INTRODUCTION

Alzheimer’s disease (AD) is considered as the primary cause of dementia in people with age 65 and above, and it appears to be more prevalent in every decade of life¹. World Health Organization says that it is an age-associated disease and was estimated to affect 1 in 85 people by 2050. It was reported to affect 450 million people around the globe irrespective of the geography²&³. It affects the neuronal cells in the specific brain region, producing difficulties...
with memory, rare behavior, struggle in thinking, and finally leads to death. The cholinergic neuron transmission was found to be affected in the brain leading to the significant role in learning and memory.

Diabetes has been approved as one of the quickly emerging global health concern in the 21st Century. It was estimated that around 463 million adults of age between 20 and 79 years are presently living with DM. The countries such as China, India and the United States are likely to stay on the most prevalent countries in 2030 also. In India, it was anticipated that the number of diabetes affected people to increase from 77 million (2019) to 101 million by 2030 and further to 134 million by the end of 2045. It is predicted that management cost of treatment of DM will be around $825 billion by 2030 and will reach $845 billion by 2045. In recent times, there has been some correlations reported about the neurological complications of DM, such as cognitive impairment, vascular dementia, stroke, or depression, though the mechanisms associated have not been completely established.

It’s been observed that the brain tissue of the diabetic patients with controlled or uncontrolled hyperglycemia have shown injury at various locations with a varied profile of micro and macrostructural changes, which leads to the neurodegeneration, neurovascular deterioration, neuro-inflammation, and progressive cognition decline. This establishes the correlation between the DM and AD associated clinical symptoms in the patients affected with DM.

Sesbania grandiflora Linn belongs to the family of Fabaceae, it is known as hummingbird tree or scarlet wisteria. It is majorly found in India or Southeast Asian regions, and it requires hot and humid areas for cultivation initially. The Sesbania grandiflora plantations were cultivated in Krishnagiri district, Tamil Nadu state in the month of October. Sesbania grandiflora Linn (SGL) leaves were collected in the month of February 2020 from Chittoor district, Andhra Pradesh, India.

**MATERIALS AND METHODS**

**Plant Materials**

Sesbania grandiflora Linn (SGL) leaves were collected in the month of February 2020 from Chittoor district, Andhra Pradesh, India.

**Drugs & Chemicals**

Piracetam obtained from Alkem Laboratories Ltd, Metformin as gift sample from Cipla Pharmaceuticals, Diagnostic Kits purchased from Bio Lab, India, and Streptozotocin were bought from Sigma Aldrich, India.

**Selection of Animals**

From mahaveer enterprises, selected wistar rats of 150 to 200 gm and albino mice of 20 to 25 gm of both sexes were procured and maintained under standard laboratory conditions (25±1°C, 55±10% & 12 hrs light to dark cycle) and fed with usual pellet diet and water ad libitum. The experimental procedures were followed after getting the ethical approvals from the institute with reference number CPCSEA/IAEC/VCOP/19/8/12.

**Preparation of the Extracts**

Sesbania grandiflora leaves collected and washed, sliced to small pieces, exposed to shade-drying, pulverized, and extracted with increasing polarity from petroleum ether (PE), ethyl acetate (EA) and methyl alcohol (MA) for 12 h at 50°C using a Soxhlet apparatus. The resultant extract was transformed into 2% sodium carboxymethyl cellulose (CMC) mixture employing mortar and pestle for further studies.

**Phytochemical Investigation**

Selected plant extracts were carried out for evaporation to get residue and adding dilute Hydrochloric acid to it. Consequently unsteady and then filtered. This filtrate used for carrying disorders and numerous compounds have exhibited antioxidant, anti-inflammatory and neuroprotective properties. The current work is aimed to explore the natural compounds obtained from the Sesbania grandiflora plant for neuroprotective activities, by considering the various therapeutic targets: inflammation, oxidative stress, vascular damage, or cognitive impairment.
out the identification tests for numerous phytochemical constituents\(^22\).

**Acute toxicity study**

As per the OECD-423 acute toxicity test was performed by using three mice for each step. The doses of 5, 50, 300, and 2000 mg/kg per oral route were chosen as four fixed-dose levels\(^23\).

**Grouping of Animals**

Total 60 wistar rats (100-120 gm) existed arbitrarily split up into ten distinct groups, each group having 6 rats and treated with following intervention for 71 consecutive days (Table 1).

Group I, consisting of 6 rats which was given with 2% solution of Sodium CMC orally and acting as a control group. To the Group II animals, along with 2% Sodium CMC, Streptozotocin also was administered orally, which serves as disease control group. Group III animals were used for standard drug Metformin treatment (oral administration) followed by Streptozotocin administration. Group IV was given with Piracetam (oral administration) along with Streptozotocin. Group V and VI received the PEESGL 100 & 200 mg/kg respectively followed by Streptozotocin. Group VII and VIII were given with EAESGL 100 & 200 mg/kg respectively and after 70 days of Streptozotocin administration. Group IX and X received MAESGL 100 & 200 mg/kg was dispensed orally 70 days followed by Streptozotocin\(^24\).

**Experimental Procedure**

**Induction of Diabetes**

For diabetes induction the overnight fasting animals were divided into 10 groups (n=6), 55 mg/kg of streptozotocin (STZ) (intraperitoneal) was chosen to induce disease to the experimental animals. The glucose levels in blood were estimated after 48 hrs by the GOD-POD method the blood glucose level greater than 250 mg/dl of reflected as diabetic\(^25\&26\).

**Spontaneous Alteration Behavior in Y-Maze Test**

The Continuous impulsive alternation behaviour of rats was observed by using Y-maze test. It made up of plastic with three arms of dimensions 36 × 7 × 13 cm spreading like a trigonal planar structure from the central core with 120º each. Every subject was kept at the corner of one arm and permitted to travel easily from end to end in the Y maze for the period of 8 min. Entry of arm was clear when the 4 paws into one arm. The entry into the arm confirmed visually and noted. If the animal made numerous entries into any arm (A, B, C) was considered as an alternation on overlapping triplet sets. The spontaneous alternation percentage was estimated on day 71 & 75 by the below equation\(^27\):

\[
\text{% of Alternation} = \frac{\text{(number of alternation)}}{\text{(total arm entries-2)}} \times 100.
\]

**Morris Water Maze**

Wistar rats were accustomed to find immersed stage (6.5 cm diameter and 1 cm below the water surface) in a rounded pool (60 cm diameter & 30 cm height) occupied by turbidity water. Outside visual hints were situated over the pool to navigate the animals in such a predetermined manner. The immersed platform was immovable at SW (south-west) path. Head start varied between NE (north-east), SE (south-east), and NW (north-west) path in a pseudo-random style. Every animal was positioned in the water in front of the wall of the pool and supported to swim to reach the platform for about 60s. Locating the platform was distinct as existence intelligent to remain on it for minimum 2s; rat that cross over the platform devoid of discontinuing (leaping instantaneously back into the water) were allowed to swim till the end of the trail.

When the rat unsuccessful in discovering the platform in allocated time, the rat was manually placed onto the platform and considered as a latent time of 60s. After each trail, the rats were dehydrated with cloth and allowed to rest for 5 minutes and allowed for next trail.
Table 1: Grouping of animals for the experimentation.

<table>
<thead>
<tr>
<th>S. No</th>
<th>Group</th>
<th>Treatment</th>
<th>Dose (mg/kg)</th>
<th>No of rats</th>
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<tbody>
<tr>
<td>1</td>
<td>Group I</td>
<td>Control</td>
<td>NIL</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>Group II</td>
<td>Streptozotocin</td>
<td>55</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>Group III</td>
<td>Metformin+Streptozotocin</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>Group IV</td>
<td>Piracetam+Streptozotocin</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>Group V</td>
<td>PEESGL+Streptozotocin</td>
<td>100</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>Group VI</td>
<td>PEESGL+Streptozotocin</td>
<td>200</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>Group VII</td>
<td>EAESGL+Streptozotocin</td>
<td>100</td>
<td>6</td>
</tr>
<tr>
<td>8</td>
<td>Group VIII</td>
<td>EAESGL+Streptozotocin</td>
<td>200</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>Group IX</td>
<td>MAESGL+Streptozotocin</td>
<td>100</td>
<td>6</td>
</tr>
<tr>
<td>10</td>
<td>Group X</td>
<td>MAESGL+Streptozotocin</td>
<td>200</td>
<td>6</td>
</tr>
</tbody>
</table>

PEESGL: Petroleum Ether Extract of SGL Leaf; EAESGL: Ethyl Acetate Extract of SGL Leaf; MAESGL: Methyl Alcohol Extract of SGL Leaf.

Rats executed four successive trials per day completed a 4-day training period. The time taking to reach the target is the escape latency for each rat was documented manually. On the last day a probe trail was approved. Each rat underway at NE can swim easily for 60s. memory retaining was determined by measuring the time to reach the target platform.

Neurotoxicity Studies
For neurotoxicity studies experimental animals were sacrificed and brain was removed and weighed. For brain homogenization, 20 mg of the brain tissue was suspended per ml of cold pH 7.4 phosphate buffer and centrifugation was done at 800 rpm for 5 mins at 4 °C to split the nuclear fragments and again performed the centrifugation at 1050 rpm for 20 minutes at 4 °C to get the supernatant. This supernatant was utilized for biochemical parameters estimation.

Estimation of Acetylcholinesterase (AChE)
Ellman’s method was employed for the estimation of neurochemical (AChE) assessment. 0.4 ml of supernatant layer of the brain homogenate, 2.6 ml of phosphate buffer (pH 8) and 100 µL of DTNB (5,5′-dithiobis-(2-nitrobenzoic acid)) and then the absorbance was measured by a spectrophotometer at 412 nm wavelength. 20 µL acetylthiocholine-iodide was taken as substrate for the enzyme and noted the alterations in absorbance for a period of 10 mins at intervals of 2 mins. Difference in the absorbance per min was dignified and acetylcholinesterase activity was stated as µM/l/min/gm of tissue.

Assessment of anti-oxidant activity of plant extracts
According to method of Wills the lipid peroxidation of plant extracts was evaluated. The development of malondialdehyde (MDA) is critical for thiobarbituric acid reactive substance levels and it is quantified in MDA/mg of the protein.

Total nitric oxide levels
The 500 µl of Greiss reagent was added to supernatant liquid (100 µl) and the resultant solution absorbance was estimated at 546 nm. The amount of nitrite was measured by using sodium nitrite standard curve and it is stated as ng/mg of the protein.

Superoxide dismutase (SOD) levels
According to the method of Kono, SOD levels were assessed and for the supernatant layer (100 µl), added the sodium carbonate (1ml), of nitroblutetrazolin (0.4 ml) and of ethylene diamine tetra acetic acid (0.2 ml) and the corresponding absorbance was determined at 560 nm and is expressed in µg/mg of protein.

Catalase (CAT) levels
According to the method of Claiborne the CAT levels were assessed. A supernatant of 100 µl added with 1.9 ml of phosphate buffer measure the absorbance at 240 nm and it is specified as µg/mg of protein.
Glutathione (GSH) levels
According to the method of Jollow the GSH levels were assessed. The GSH levels were estimated spectrophotometrically at 412 nm and stated as ng/mg of protein.

Results Analysis
The data were articulated in Mean ± SD. The result was evaluated through one-way ANOVA and followed by Tukey’s comparison tests with GraphPad Prism 5.0 and p value < 0.05 must be deliberated as significant.

RESULTS AND DISCUSSION

Result
Acute toxicity studies
Up to 2000 mg/kg of S. gradiflora extracts did not show any death or illness were perceived in various doses for 14 days. Hence, the median lethal dose (LD₅₀) of SG was greater than 2000 mg/kg. The results of acute toxicity study showed no clinical signs of toxicity and mortality in the SG treated animals even after administration of 2000 mg/kg dose. Hence, as per OECD guidelines lethal dose was assigned to be more than 2000 mg/kg. 1/20th and 1/10th of this lethal dose (i.e. 100 mg/kg and 200 mg/kg) were taken as effective doses for the study.

Preliminary Phytochemical Analysis
The phytochemical screening of leaf extracts of S. grandiflora was investigated for the secondary metabolites such as alkaloids, glycosides, flavonoids, tannins, steroids, terpenoids, carbohydrates and proteins. The preliminary phytochemicals recognized the presence and absence showed in Table-2.

Table 2: The Qualitative Determination of Phytochemicals in Pet Ether, Ethyl acetate and Methanol of S. gradiflora.

<table>
<thead>
<tr>
<th>Phytochemical</th>
<th>Pet ether</th>
<th>Ethyl acetate</th>
<th>Methanol</th>
</tr>
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<tbody>
<tr>
<td>Alkaloids</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Glycosides</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Tannins</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Steroids</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Tri Terpenoids</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Protein</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>+</td>
<td>+</td>
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</tr>
</tbody>
</table>

Nootropic Activity
Y-Maze Test
The outcomes obtained for the effect of S. gradiflora leaf extracts for the percentage of spontaneous alternation in Y-maze are showed in Figure 1. The control group was compared with the disease control group (STZ-induced) and induction of amnesia was significantly established (***p< 0.001). After the administration with S. grandiflora, assessed against disease control group Piracetam (5mg/kg), EASGL (200 mg/kg) MASGL (100 and 200 mg/kg) fed animals demonstrated a substantial (**p< 0.01) improvement in memory and learning ability on Day 71 and 75.

Morris Water Maze Test
Transfer Latency of S. grandiflora leaf extracts on tested animals through morris water maze was showed in Figure 2. The transfer latency of disease control group (STZ-induced) is significantly (**p<0.001) increased in contrast to the control group. Once treatment with S. grandiflora, compared with disease control group Piracetam (5mg/kg), EASGL (100 and 200 mg/kg) MASGL (100 and 200 mg/kg) treated animals showed a significant (***p< 0.001) reduction in transfer latency on Day 75. On day 71 also shows significant decrease in transfer latency were observed.

Estimation of Acetylcholinesterase (AChE)
The action on AChE existed significantly (**p< 0.001) decreased by Piracetam, EASGL and MASGL with the doses of 100 and 200 mg/kg of when compared with disease control group (Figure 3).

Assessment of anti-oxidant activity of plant extracts
The outcomes of lipid peroxidation shown in STZ administered group stated significantly rise in the levels of MDA (**p<0.001) in contrast to the control group. S. gradiflora treatment, EASGL (100 and 200 mg/kg) significantly inhibited (**p< 0.01), whereas MASGL (100 and 200 mg/kg), Metformin (10 mg/kg) and Piracetam (5 mg/kg) treated animals showed more significantly (**p< 0.001) inhibited the MDA level in diabetic rats (Figure 4).
Fig. 1: Spontaneous alterations of *S. grandiflora* extracts in STZ induced amnesia Rats.

Fig. 2: Transfer latency of *S. grandiflora* extracts in STZ induced amnesia Rats.

Fig. 3: Effect of *S. grandiflora* Acetyl choline esterase activity in STZ rats.

Fig. 4: TBARS levels in brain tissue.
**Effect on nitrosative stress**

Levels of Nitrite were considerably (\(a*** p < 0.001\)) raised in the brain tissue of STZ administered rats when matched with control group. *S. grandiflora* extract of EASGL administration in 100 and 200 mg/kg doses substantially inhibited (\(b** p < 0.01\)), whereas MASGL (100 and 200 mg/kg), Metformin (10 mg/kg) and Piracetam (5 mg/kg) treated rats displayed more significant (\(b*** p < 0.001\)) effect on the NO level in inhibition in diabetic rats (Figure 5).

**Catalase enzyme level in the brain tissue**

Estimation of brain CAT activities significantly (\(a*** p < 0.001\)) diminution in the in diabetic induced group when compared with the control, while *S. grandiflora* treatment, EASGL (200 mg/kg), MASGL (100 and 200 mg/kg), Metformin (10 mg/kg) and Piracetam (5 mg/kg) treated rats demonstrated more significantly (\(b*** p < 0.001\)) increase the CAT in diabetic rats (Figure 6).

**SOD effect in the brain tissue**

The SOD formation was considerably decreased in the brain tissue of the STZ treated rat (\(a*** p < 0.001\)) when compared with control. Administration of *S. grandiflora* extracts of EASGL (200 mg/kg), MASGL (100 and 200 mg/kg), Metformin and Piracetam treated rats indicated more significantly (\(b*** p < 0.001\)) increase the SOD effect in diabetic rats (Figure 7).

**GSH level in the brain tissue:**

Assessment of GSH levels showed a considerable reduction in the STZ group compared to the control rat (\(a*** p < 0.001\)). Administration of *S. grandiflora*, EASGL (200 mg/kg), MASGL (100 and 200 mg/kg), Metformin and Piracetam treated rats demonstrated more significantly (\(b*** p < 0.001\)) increase the GSH effect in diabetic rats (Figure 8).

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![Fig. 5: Total Nitrite levels in brain tissue.](image)

![Fig. 6: Catalase enzyme level in the brain tissue.](image)
Discussion

For Alzheimer’s disease, currently there is no treatment available and the present medications existing is only palliative treatment with limited efficacy. The application of alternative medication such as herbal extract produces a broad approach to the management of neurological conditions such as AD. Truly, numerous reports of scientific experiments have indicated that the consumption of several remedial plants and the extracts of bioactive elements for the cure of AD. While the precise molecular mechanism is still not known, the phytochechemical evaluation of the various parts of the plants must revealed the existence of numerous valuable secondary metabolites, that display an extensive range of pharmacodynamic actions, including anti-cholinesterase, anti-inflammatory, hypolipidemic and antioxidant properties. The current study deals with the *S. grandiflora* leaf extracts were given for 70 days to the animals and the neuroprotective action in methanol-induced animal model of cognitive impairment and corresponding oxidative stress were investigated.

The current investigation analyzed the impacts of *S. grandiflora* solvent extracts treatment on memory loss, oxidative stress, and cholinergic transmission impairment in chemically induced (i.e., STZ) animal model of diabetes in mice. Previous investigations have proposed that DM is associated with various neurological impairments in the focal sensory network like cognition and learning capabilities. STZ can induce type 1 or type 2 diabetes depending on the concentration used. In this present investigation, the intention is to get not exclusively the diabetes type of model, and to those additional defects in memory was also considered. Chemically STZ is a glucosamine-nitrosourea derivative, have got anti-microbial properties and found to be poisonous to the pancreatic cells and is used to produce exploratory diabetic condition in experimental animals. When STZ administered through the intraperitoneal routes, it creates cognition impairment and enhances cerebral masses of Amyloid β and tau protein. STZ...
injection can produce the AD like pathophysiological condition in animal brain by causing the neuroinflammation and oxidative stress, which is the suitable experimental model\(^{41}\). Moreover, the treatment of STZ causes the brain cells to become insulin-resistant, which produces the normal dementia like condition with loss of memory, progressive cholinergic deficiencies, carbohydrate hypometabolism, stress due to reactive oxygen species (ROS), and finally neurodegeneration\(^{42,43}\).

There are various reports of the neuroprotective properties of various phytoconstituents helps in the management of neurological disorders along with associated mood disorders and memory related problems. Results of present study showed significant improvement in spatial reference memory and transfer latency, suggesting of nootropic activity of SGL extracts in diabetes induced cognitive decline models. Oxidative stress in brain generates oxygen radical like superoxide anion, hydroxyl radical, and hydrogen peroxide, which act on polyunsaturated fatty acids in brain, thereby propagating the lipid peroxidation. The major antioxidant and oxidative free radical scavenging enzyme like GSH, SOD and catalase plays an important role to reduce oxidative stress in brain. Oxidative damage to various brain regions constitutes the long-term complications, morphological abnormalities and memory impairments. In the present study, TBARS levels were significantly increased (P<0.001) whereas GSH, SOD and CAT levels were markedly reduced in the brains of diabetic control. Treatment with SGL extracts significantly reduced the levels of TBARS, whereas GSH, SOD and CAT levels were increased. Therefore, SGL might have protective effect against diabetes induced cognitive decline due to reduced oxidative stress. The antioxidant properties of SGL might help to ameliorate the cognitive dysfunction in diabetic animals.

The neurotransmitter acetylcholine is degraded by the enzyme AChE. Therefore, the use of AChE inhibitors is the most effective pharmacological approach for the symptomatic treatment of AD. We observed a significant rise in AChE activity in the brain of diabetic rats. Treatment with MM attenuated increase in AChE activity in the brain of diabetic animals. Hence, SGL extracts treatment ameliorated cognitive decline, cholinergic dysfunction, reduced oxidative stress, and NO in the diabetic animals which may find clinical application in treating neuronal deficit in the diabetic patients. STZ causes the oxidative stress by fundamentally expanding the MDA levels and diminishing the GSH level. Besides, the nitrite levels in the brains of control group are fundamentally increased. This increment in the oxidative pressure might be expected to uncontrolled hyperglycemia occurrence in brain after STZ injection. The brain tissue of STZ treated animal are referred to show diminished glucose consumption when contrasted with the control group animals, prompting hyperglycemic condition\(^{43}\). Due to the high oxidative stress, enhanced free radicals caused the increase in Nitrite level\(^{44}\). Hyperglycemia incites up-regulation of iNOS and equal increment in production of superoxide triggers the formation of pro-oxidant, peroxynitrite, which amplifies the oxidative strain\(^{45}\).

The treatment of STZ fundamentally increased the MDA levels and the corresponding series of lipid peroxidation in the animal brain. Here, it was also observed that the rise in lipid peroxidation is correlated with the reduced levels or activity of the antioxidants like glutathione peroxidase and catalase, it was evident in the current study. These results are aligned with the previous studies, which recommend that the antioxidant compound capacities diminished in the brain during persistent diabetic neuropathy\(^{46}\). The diabetic induced animal models, shown reduced synaptic versatility and obstructed exhibitions in behavioral learning tasks, and a decrease in diabetic animal performance, for example, Morris water maze and Y-maze\(^{47}\). From the above result it was concluded that diabetes induced cognitive decline was improved by the treatment with SGL leaf extracts in rats and further investigation is needed to know the exact mechanism of cognition for developing lead compounds and to overcome the limitations of the current work.

**Conclusion**

In the Current investigation, the treatment of extracts of *S. grandiflora*, to the diabetic animals, enhanced the spatial memory and
condition avoidance memory. It was observed that there is an improvement in the memory augmentation after the STZ induced disorder condition with the plant extract treatment. Whereas the vehicle treated animal group have shown the memory deficit even after 20 days of treatment. In addition to that we have studied the impact of S. grandiflora on spatial navigation memory in diabetic induced mice by cross-arm maze. We observed that diabetes could altogether reduce the real alternation percent as an index; nonetheless, oxidative stress might add to spatial navigation memory in hyperglycemia condition. In this, we found that S. grandiflora extracts could increase the alternation percent in the cross-maze test, but no alteration in locomotor activity. Treatment with S. grandiflora extended the locomotor movement and the alternation percent in diabetic rats; though, S. grandiflora increased the alternation percent yet didn't modify the locomotor action in non-diabetic rat. This logical inconsistency shows that increasing impact of S. grandiflora on actual alternation score couldn't be an outcome from the locomotors action is lower in diabetic animals. Moreover, the data from the Morris water maze test additionally affirm the impact of S. grandiflora enhancing effect on increasing the spatial memory in diabetic and non-diabetic animals.

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Conflict of Interest
Authors declare no conflict of interest

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التقييم الدوائي لنشاط منشور الذهن والوقاية العصبية لمستخلصات نباتات سيسينيئا جرانديفولو، في نموذج الجرذان المصاب بمرض السكري الناجم عن السطروتوتوسينين

جاجديشوار كولجوري 1 - سوبهارا راجو راباكا 2 - رامان كرارا ردي الاشارالإله
- كوتشاروا رو جسن 3 - شيريشا يويايتي 3 - راغافندرا كومار جوندا 4

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4 قسم العلوم الصيدلانية ، مؤسسة فنجان للعلوم التكنولوجيا والبحث ، فادلامودي، جونتور، ولاية انديانا، براديش، الهند، 522213

التخلفية: داء السكري (DM) هو اضطراب متعدد العوامل وغالبًا ما يرتبط بالمشاكل المزمنة المرتبطة بالأعصاب الرئيسية المختلفة. في الأونة الأخيرة، تم الإبلاغ عن بعض الارتباطات حول المضاعفات العصبية لمرض السكري، مثل ضعف الإدراك أو الخرف الوعائي أو السكتة الدماغية أو الالتهاب.

ولاحظ أن انسيج دماغ مرضى السكري الذين يعانون من ارتفاع السكر في الدم قد أظهرت إصابة في مواقع مختلفة مع مجموعة متنوعة من التغيرات الدقيقة والبيئية الكلية، مما يؤدي إلى التهاب العصبي، وتدهو أنواعية الدمية العصبية، والالتهاب الأعصاب، وتدهو الإدراك التدريجي.

الهدف: تقيم الدراسة الحالية نشاط تفعيل الذاكرة لمستخلصات نباتات سيسينيئا جرانديفولو (SG) في نموذج الفئران المصاب بالسكري الناجم عن السطروتوتوسينين (STZ).

الطريقة: تم تحليل المستخلصات (الأثيل البترولي)، أسئلة البترولي، من أجل السمية الحادة، وفما بعد ثم تحليل مستخلصات الوقاية العصبي وتعزيز الذاكرة في نموذج الفئران المختبر. تم إعطاء حقيقة SG (50 مجم / كجم) داخل الصافاق للحيوانات للبحث على ضعف الذاكرة. تم إعطاء مستخلصات STZ (55 مجم / كجم) داخل الصافاق للحيوانات للبحث على ضعف الذاكرة. تم إعطاء مستخلصات STZ لفترة 20 يومًا، مما تلقى خفضًا في مستوى الذاكرة. تم تحليل وظيفة كويلينية وتاثير ضغط الأكسيد للأنسجة المحيطة. النتائج: لاحظ أن STZ تسبب في ضعف كبير في الذاكرة، والذي تم عكسه بشكل كبير بواسطة المستخلص الميثانولي بنسبة 100 و 200 مجم / كجم، وجد أن الفئران الضوئي كويليني، وارتفاع مستويات بروكسيمتيان الدهون قد انخفض بشكل ملحوظ (P<0.001) في المجموعة المضادة بمرض
السكري، تم تحديد أن هناك انخفاضًا في أنشطة الجلوتاثيون سوبر أكسيد ديميوتاز، والكتلاز مقارنة بحيوانات المجموعة الضابطة.

الخلاصة: أثبتت الدراسة الحالية أن مستخلصات أوراق SG تعمل على تحسين الذاكرة عن طريق تعزيز انتقال الكوليني وتقليل الاكسدة في مخ الجرذان المصابين بداء السكري.